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COVID19 in South Asians/Asian Indians: Heterogeneity of data and implications for pathophysiology and research

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ABSTRACT

Despite a large population and limited health infrastructure, the incidence and mortality of Coronavirus Disease 2019 (COVID-19) has been lower in South Asia than many regions. The underlying reasons and mechanisms for this relative protection are not established. However both genetic and environmental factors might play a role. Polymorphisms in ACE2 gene, ACE gene and in genes for some of the host cell proteases could affect the viral entry and replication. There is some evidence that HLA polymorphisms and several pathways involved in immune and inflammatory response could contribute to ethnic variation. Cross immunity because of past exposure to viral infections as well as malaria is likely to protect from the severe manifestations of disease. Role of BCG vaccination in trained innate immunity is recognised and could be a protective factor against COVID-19. There is limited evidence of the possibility of a less virulent viral strain circulating in South Asia. There is evidence from different parts of the world that temperature and humidity can influence viral survival as well as the host immune response. Finally implementation of early containment measures by some South Asian countries has also contributed to a less disease burden.

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1. Introduction

Coronavirus Infectious disease (COVID-19) pandemic has affected more all parts of globe with more than five and a half million confirmed cases and more than 340,000 deaths. However, there are significant differences in the prevalence, morbidity, severity and mortality among different countries and in different regions in the same country. Some of these variations could be ascribed to social, behavioural, cultural, and economic factors, as well as health infrastructure, access to healthcare and political and public health response. The major epicentres of the COVID-19 pandemic are United States of America (USA) and parts of Europe with the highest number of cases, case fatality rates and deaths per 100,000 population (Table 1) [1]. On the other hand, many countries in Asia and Africa have less incidence and severity of this disease.

South Asia has been dealing with multiple health issues which include non-communicable diseases like diabetes,

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Table 1 – Top 20 countries leading in deaths per 100,000 population due to COVID-19 (Till May 25, 2020).

Country	Deaths per 100,000 population	Confirmed cases	Deaths	Case fatality (%)
Belgium	80.65	56,511	9,212	16.3
Spain	61.27	234,824	28,628	12.2
United Kingdom	55.64	262,547	36,996	14.1
Italy	54.40	230,158	32,877	14.3
France	42.49	183,067	28,460	15.5
Sweden	39.57	33,843	4,029	11.9
Netherlands	33.94	45,647	5,849	12.8
Ireland	33.09	24,698	1,606	6.5
USA	30.02	1,662,302	98,220	5.9
Switzerland	22.46	30,746	1,913	6.2
Ecuador	18.75	37,355	3,203	8.6
Luxembourg	18.10	3,993	110	2.8
Canada	17.96	87,119	6,655	7.6
Portugal	12.94	30.788	1,330	4.3
Peru	11.34	123,979	3,629	2.9
Brazil	11.20	374,898	23,473	6.3
Germany	10.02	180,600	8,309	4.6
Denmark	9.71	11,586	563	4.9
Iran	9.11	137,724	7,451	5.4
Panama	7.42	1,183	310	2.8

hypertension, obesity and heart disease as well as communicable diseases like tuberculosis, malaria, periodic outbreaks of dengue, viral encephalitis etc. Coupled with that is high prevalence of malnutrition in the population and limited health infrastructure and manpower. Comorbid conditions like diabetes and heart disease are known to worsen the disease course in COVID-19 [2]. Despite these limitations, the incidence and severity of COVID-19 in South Asia is lower than the Western world. Though studies on racial variations and differences have largely focused on non-communicable diseases, it is possible that there are some biological factors which determine not only the differences in susceptibility to COVID-19, but also the severity in different populations. Additionally, environmental factors like temperature, humidity and pollution could have an influence on modulating the transmission dynamics, viral survival and host immune response. Potential mechanisms for these differences and ethnic variations in host responses to COVID19 are discussed.

2. Epidemiology

South Asia has shown less disease burden than many parts of Europe and North America in terms of total number of cases (Tables 1 and 2). One of the reasons being put forth for relatively fewer cases in South Asia is a lower rate of testing. Tests per one thousand population till May 25, 2020 were 2.2 and 1.54 respectively, in India and Bangladesh as opposed to 172 and 57.5 respectively, in Iceland and Italy [3]. One more indicator of the burden of disease is the number of tests conducted per confirmed case of COVID-19 and this figure is higher in India than in countries with high number of confirmed cases like Italy and USA (21.8, 15.2 and 8.7, respectively) [3]. This means that India is conducting more tests to detect a positive individual than US and many other countries, implying a lower disease burden.

Case fatality rate which is the ratio of deaths and total number of cases is also much lower in all parts of South Asia [1]. This has to be interpreted in light of lower testing rates; the case fatality rate would actually be much lower had more tests been carried out in countries in South Asia. A more useful and unbiased indicator to assess the disease severity is mortality rate in relation to the population size. It is noteworthy that the mortality rate per 100,000 population in all countries in South Asia is far less compared to the western nations [1] (Tables 1 and 2). The demography of South Asia with a lower proportion of elderly individuals than Western nations (proportion of elderly in population 5.2, 6.2 and 22.8 per cent, respectively in Bangladesh, India and Italy) is possibly one factor responsible for a lower disease burden and mortality [4].

Table 2 – Cases and mortality of COVID-19 in South Asia (Till May 25, 2020).

Country	Deaths per 100,000 population	Confirmed cases	Deaths	Case fatality (%)
Pakistan	0.55	56,349	1,167	2.1
India	0.31	144,950	4,172	2.9
Bangladesh	0.31	35,585	501	1.4
Sri Lanka	0.05	1,182	10	0.8
Nepal	0.01	682	4	0.6

Most of the data on COVID-19 in people of Asian origin living abroad has come from USA. In New York City, age adjusted rates per 100,000 population of non-fatal hospitalized COVID19 cases were lower in Asians compared to other races (132.6, 162.5 and 379.9 in Asians, Whites and Blacks respectively). Age adjusted rate per 100,000 population of fatal cases was also lower in Asians (90.8, 107.7 and 209.4 respectively) [5]. Another way of looking at the mortality data is that Asians represented 7% of deaths due to COVID-19 while they comprise 14% of population of New York. Similar findings were reported in the state of Connecticut, USA, where Asians comprised 2.9% of 3141cases and 2.2% of 96 deaths against the prevalence of 4.9% in general population [6]. In a recent analysis of data from 322 counties in USA, though the odds ratio for mortality for Asians was 0.77 compared to Whites, it was 0.98 after adjustment for age and geographical calculation [7].

Preliminary reports about COVID-19 in Asians from the United Kingdom (UK) are at variance with findings in native South Asians or from those living in North America. Two thirds of 106 healthcare workers in National Health Service (NHS) who died from COVID-19 were from an ethnic minority background, and at least half were not born in the UK [8]. Data from the Intensive Care National Audit and Research Centre showed that 54.4% of Asians admitted to critical care units died compared to 46.7% of whites [9]. In a study from the UK Biobank cohort (more than 500,000 patients) in which 1474 hospitalised patients were tested for COVID-19, white ethnicity was associated with lower chances of a positive test than non-white ethnicity(Odds Ratio 0.488 [CI0.340–0.696, P = 0.0000875]) [10]. Another analysis of 348,598 UK Biobank participants, of which 449 had confirmed COVID-19 infection, found South Asian ethnicity to be associated with increased risk of COVID-19 compared to white ethnicity (OR 2.65[1.65–4.25], $p < 0.001$) [11]. One study in Oxford, UK in 3802 patients presenting with respiratory symptoms found increased positivity for SARS CoV2 in Asians (Adjusted OR 1.46 [0.94–2.29], $p < 0.0001$) [12]. However a recent report did not find increased positivity for COVID-19 in Asians with Asians comprising 6.5% of first 381 patients confirmed to have COVID-19 in Great Britain compared to their proportion in general population of 7.5% [13].

The reasons for these differences in data from South Asia, South Asians in USA and those in UK are not clear. Socioeconomic factors, overcrowding at home and late presentation to healthcare facility leading to late presentation and relatively higher viral loads could be some of the contributing factors.

3. Plausible biological factors which may cause variations in COVID-19 incidence and severity

Pathogenesis of COVID-19 involves the entry of virus into cell, recognition by immune cells of the host and immune and inflammatory response. There are individual and ethnic variations in the host response and mutations have been identified in the virus which may affect its virulence or transmissibility.

3.1. *Differences in viral binding to host Cell:*

Angiotensin converting enzyme-2(ACE2) Expression: ACE2 serves as the receptor for severe acute respiratory syndrome coronavirus-2 (SARS CoV2) and is also involved in modulating the effect of virus on lung injury. Ethnic variations in the amount of ACE2 expression in type 2 alveolar epithelial cells have not been studied in detail, though a preliminary analysis of 4 datasets from lung cancer patients did not find any difference in ACE2 expression among Asians and Caucasians [14].

An analysis of the coding-region variants in ACE2 gene failed to identify any naturally occurring coronavirus S-protein binding-resistantACE2 mutants in different populations; however low-frequency missense variants affecting the S-protein binding in different ethnic groups cannot be ruled out [15]. Interferon has been shown to increase ACE2 expression [16] and ethnic variations in host interferon response could be a key factor in modulating viral replication after infection [17].

One of the factors influencing ACE2 expression is the circulating and tissue concentrations of ACE, with an inverse relationship between these two enzymes. The angiotensin-converting 1 (ACE1) enzyme is characterized by a genetic deletion/insertion (D/I) polymorphism in intron 16 [18]. The D allele is associated with higher ACE levels and a reduced expression of ACE2. Ethnic variations in the frequencies of these alleles have been reported. In a study in London, there was a much higher frequency of the II genotype in those of South Asian origin than in whites and those of African descent (39.8%, 18.4% and 18.4%) [19]. An analysis of the polymorphisms in 25 European countries found that prevalence as well as severity of COVID-19 correlated inversely with the ACE D allele frequency and about 38% of the variability of the prevalence could be explained by the relative frequency of the ACE1 D-allele [20].

A Disintegrin and Metalloproteinase 17 (ADAM 17) Activity: ADAM 17 is a protein involved in the shedding of several membrane proteins important for immunity and inflammation like tumor necrosis factor alpha, intercellular adhesion molecule-1, and ACE2. ADAM17 expression and activity is increased in patients with sepsis. In a study in Han Chinese patients with sepsis, functional polymorphism of ADAM17 was observed with certain alleles associated with increased ADAM17expression and increased production of pro-inflammatory cytokines like IL6 and IL-1β [21]. Though polymorphisms of ADAM17 have not been studied in South Asians, polymorphisms of a related protein ADAM10 have been reported in Indian patients with asthma [22]. Therefore, possibility of polymorphisms of ADAM17in South Asians influencing both ACE2 levels and the inflammatory response to viral infection cannot be ruled out.

Host Cell Proteases: Host cell proteases, namely transmembrane serine protease (TMPRSS), furin, trypsin, plasminogen and others, have a crucial role in viral entry by causing the cleavage of S protein and triggering its binding to the receptor. Co expression of ACE2 and TMPRSS in type 2 alveolar cells is important for viral entry and replication. Mutations in furin, TMPRSS and plasminogen genes having functional implications have been described, however, their distribution in

different ethnic groups needs to be studied [23]. Polymorphisms of furin gene have been shown to affect the seroconversion of patients with Hepatitis B infection in Han Chinese [24].

Micro RNA: The micro RNAs (miRNA) are small noncoding RNAs that function as guide molecules in RNA silencing and may regulate gene expression. A unique miRNA, named hsa-miR-27b was found to target the mutation found in the SARS CoV2 genome isolated from India [25]. Importantly, hsa-miR-27b is known to inhibit ACE expression which would indirectly increase ACE2 expression [26]. Also, cells overexpressing miR-27b were shown to decrease replication of human immunodeficiency virus-1 (HIV-1) [27].

Androgens: Reduced ACE2 expression has been seen after orchiectomy in rats [28]. TMPRSS2 exhibits increased expression upon exposure to androgens [29]. This observation raises the possibility of androgens facilitating infection with SARS CoV2. Low androgens in South Asian men compared to Caucasian men in US could theoretically contribute to lower incidence of COVID-19 [30].

3.2. *Factors implicated in differences in immune response*

HLA Polymorphisms: Human leukocyte antigen (HLA) alleles, which are critical components of the viral antigen presentation pathway, have been shown in previous studies to influence viral susceptibility and severity of disease. In infection with SARS CoV, while some studies reported HLA alleles conferring susceptibility to or protection from infection, other studies failed to find any such association [31–33]. An *in-silico* analysis of viral peptide-MHC class Ibinding affinity across 145 HLA -A, -B, and -C genotypes for all SARS-CoV-2 peptides found that though there is no correlation between the HLA allelic frequency in the population and allelic capacity to bind SARS-CoV or SARS-CoV-2 peptides, certain alleles (e.g. HLA -B*4601) could be associated with more severe infection [34]. Importantly, the frequency of HLA allele B*4601 which was found to be associated with susceptibility to SARS, was only 0.26% in Western India, compared to 13.5% in Wuhan, China [35].

Cross Immunity: Cross reactive neutralizing antibodies have been observed between different coronaviruses. Importantly, cross reactive antibodies to human coronavirus EMC were seen in patients who recovered from SARS [36]. Further, cross immunity between SARS and MERS is poor as there is only 18.6% homology between the receptor binding domain (RBD) of these two viruses [37]. Since SARS CoV and SARS CoV2 share the same receptor (ACE2), cross reactivity is expected to be higher. Indeed, there is evidence of cross-reactivity of antibodies against the spike protein of SARS-CoV-2 and SARS-CoV [38]. However, some neutralizing antibodies against the spike protein of SARS-CoV have failed to bind the spike protein of SARS CoV2. This could be because of some important differences in amino acids in the RBD of two coronaviruses [39].

Though neutralizing antibodies formed during an infection with other coronaviruses may be protective against SARS CoV2 infection; however, the phenomenon of antibody mediated enhancement (ADE) may facilitate viral cell entry and replication. Such ADE occurs when virus binds with antibodies and the virus antibody complex then binds to Fc receptors on the host cells, thereby leading to increased viral replication. There is a possibility that ADE might be contributing to the severity of infection with SARS CoV2, as these patients might have had prior infection with other coronaviruses including SARS [40]. Whether there is preponderance of protective cross-reactive neutralizing antibodies in South Asians because of prior infection with other coronaviruses, or there is a lack of ADE because of absence of cross-reactive antibodies, would be an interesting area of research.

Apart from the humoral immune response, T cell mediated immune response also plays an important role in the development of disease. T cell epitopes are highly conserved between SARS CoV and SARS CoV2 [41] and memory T cells targeting the structural proteins of SARS CoV have been reported to persist for 11 years after recovery from infection [42].Therefore, prior infection with SARS CoV may help in adaptive T cell immunity against SARS CoV2. A recent study demonstrated the presence CD4 + T cells reactive against the S-protein in 34% of SARS-CoV-2 seronegative healthy individuals. These cells targeted the epitopes in S-protein which had a homology with other coronavirus infections causing common cold, indicating cross reactivity between SARS CoV2 and other coronaviruses [43]. Though the ethnic variations in T cell response have not been studied, it is possible that frequent mild respiratory infections in South Asia impart cross reactive T cell immunity to SARS CoV2.

Heterologous immunity has generally not been seen between coronaviruses and other respiratory viruses like influenza, rhinovirus, and respiratory syncytial virus. However, cytotoxic T cells directed against human papilloma virus type 16 were found to be cross-reactive to human coronavirus OC43 [44]. A recent preprint report from Oxford, UK reported few shared CD80 + T cell cross reactive epitopes between SARS CoV2 and Influenza A virus [45]. Therefore, the protective effect of adaptive immunologic memory because of prior infections with other respiratory viruses cannot be ruled out in South Asians.

Toll-like Receptors (TLR): TLR are expressed predominantly in the host antigen presenting cells and play a crucial role in regulating the inflammatory and immune response to an infection. Polymorphisms of TLR gene have been reported in Indians and were found to be associated with susceptibility to chikangunya infection [46]. The exploration of TLR polymorphisms influencing severity of COVID-19 in South Asians would be interesting.

BCG vaccination: BCG vaccination has been shown to result in 'trained immunity' by epigenetic reprogramming at the promotor sites of genes encoding inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF) in hematopoietic stem cells in the bone marrow [47]. This trained innate immunity has been shown to protect against experimental yellow fever [48] and result in reduced parasitemia after controlled human malaria infection [49]. A study in South Africa showed that individuals vaccinated with BCG recorded a 73% reduction in respiratory tract infections compared with the non-vaccinated individuals [50]. Multiple doses of BCG vaccination resulted in a significant reduction in the number of respiratory tract infections in elderly in Indonesia [51]. A reduced risk of pneumonia with

BCG vaccination was seen in previously tuberculin-negative elderly people in a clinical trial in Japan [52].

There is a possibility that trained immunity offered by BCG vaccination might provide some resistance to the deleterious effects of COVID-19. Indeed, lower disease burden and mortality because of COVID-19 were observed in the initial weeks of pandemic in countries with universal BCG vaccination policy [53,54]. However many deviations from this general observation have been observed. An analysis in individuals born during and after the universal BCG vaccination policy in Israel did not show any difference in infection and mortality rates for COVID-19, however the analysis was limited by relatively younger age of participants [55]. Factors like BCG strain used for vaccination and the time of initiation of universal vaccination are likely to play a role [53,54].Though many countries in Europe, Asia, Africa and South America have had universal BCG vaccinations, they differ in the time of initiation of this policy [56]. For example Iran started universal vaccination in 1984 and has not seen the kind of protection form high mortality seen in countries like India which adopted universal BCG vaccination much earlier [57].One important outlier to this trend is Brazil which, despite having a universal BCG vaccination policy for a very long time has been witnessing a surge in confirmed cases and mortality. Also, countries like France and UK initiated the universal BCG vaccination in early 1950s and still had high incidence and mortality [54]. There is a possibility that there is an ethnicity specific protection offered by BCG vaccination against viral pathogens in South Asians; however role of other confounding factors needs to be studied.

Previous Exposure to Malaria: Infection with *Plasmodium falciparum* has been shown to induce trained innate immunity and causes peripheral blood mononuclear cells to hyper respond to stimulation of toll-like receptors with ligands with increased proinflammatory response [58]. However, repetitive stimulation of immune effector cells by malarial toxins could lead to cross tolerance with other antigens. Cross-tolerance has indeed been demonstrated in vitro between TLR4 (activated by bacterial endotoxin) and TLR2 (a major receptor for *Plasmodium falciparum*) [59]. It is possible that constant exposure to malaria could cause tolerance for proinflammatory response to infection with SARS CoV2 in South Asians resulting in a blunted cytokine response. A recent analysis of data from 108 countries showed negative correlation between the number of COVID-19 cases per million population and malaria endemicity of respective countries [60]. However, a notable exception is the state of Amazonas in Brazil which has a high COVID-19 mortality despite having a high incidence of malaria.

Interleukin-6 (IL-6) Polymorphisms: Levels of IL-6 are raised in patients with COVID-19 and correlate with severity of disease. Polymorphisms of IL6 gene (174G/C) have been shown to influence IL-6 levels and the frequency of C allele is found to be lower in Indians (especially North Indians) compared to Caucasians, which might be leading to less IL-6 production in Indians [61].

Vitamin D: Vitamin D deficiency has been shown to have a role in respiratory infections. Though a recent study did not find association between historically recorded vitamin D levels and incidence of COVID-19, the possibility of ethnic differences in vitamin D levels influencing the severity of COVID-19 cannot be ruled out [11].

3.3. *Viral mutations*

SARS CoV2 has also shown recurrent mutations indicating ongoing adaptation of SARS-CoV-2 to its novel human host. Recurrent, independent mutations have been identified in 198 sites in the SARS CoV2 genome based on a large-scale analysis of public genome assemblies [62]. Some of these mutations may affect the phenotype of SARS-CoV-2 and virus-host interactions. Receptor Binding Domain (RBD) of spike protein has emerged as mutational hotspot [63]. One particular mutation of an aspartate (D) at position 614 to a glycine (G) has been shown to stabilize the site in RBD making it more accessible for cleavage by host cell protease [64]. Importantly, increased case fatality rate correlated strongly with the proportion of viruses bearing G614 on a country by country basis [65].

A unique mutation (A930V (24351C > T)) in the spike surface glycoprotein of Indian SARS-CoV-2 genome was reported which was absent in other strains from Wuhan, Italy, USA, and Nepal [25]. Another mutation in S protein (R408I) mutation was identified from the SARS-CoV-2 strain in India, which represents a SARS-CoV-2 mutant with potentially reduced ACE2 binding affinity [66,67]. Mutations in genes encoding RNA dependent RNA polymerase have been identified in isolates from Europe and America and it possible some of these might be occurring in South Asians as well [68].

4. Environmental factors

a. COVID-19 Transmission and Severity: *Season, Atmospheric Temperature and Humidity:* Respiratory infections are known to show seasonal variation. One infection which shows prominent seasonality is influenza especially in temperate regions [69]. Influenza activity in South Asia has been seen all through the year with timings of peaks varying among different countries [70]. In Bangladesh, respiratory infections in children peak twice a year, once during the winter, and late in the rainy season [71]. Temperature, humidity, UV radiation and some other factors like poor food availability in certain seasons in some regions are thought to be responsible for this seasonal variability.

The effect of ambient temperature and humidity on the transmissibility of SARS CoV2 is controversial. A study done in 30 provinces in China found reduction in the incidence of cases with increase in average daily temperature and relative humidity (RH) [72]. A study in different prefectures in Japan found a significant negative correlation between air temperature and incidence of COVID-19 [73].A study analysing data from 100 Chinese cities concluded that one degree Celsius increase in temperature and one per cent increase in RH lower the effective reproductive number, R by 0.0225 and 0.0158, respectively [74]. Negative correlation between temperature and COVID-19 incidence has also been seen in Brazil and Spain, however, the temperature ranges studied were all less than 30 °C [75,76]. The pooled results of four studies mentioning the exact temperature range found that temperature

range most conducive to the survival of SARS CoV2 is 4–24 °C [77].

Contradicting the results of these studies, a study in 224 cities in China failed to show any association between temperature and cumulative incidence of COVID-19 [78]. A prospective cohort study of 144 geopolitical areas worldwide excluding China, Iran, South Korea and Italy, (375 609 cases) found no association with daily temperature, and a weak association with absolute or relative humidity (RRR per 10% 0.91, CI 0.85–0.96) and absolute humidity (RRR per 5 g/m^3 0.92, CI 0.85–0.99) [79]. Importantly, recent surge in incidence and mortality of COVID-19 in South America, especially the state of Amazonas in Brazil belies the negative linear association between temperature and COVID-19, as the temperatures in these regions are above 30°C. These environmental conditions are similar to many parts of South Asia which have not seen a similar increase in mortality. However, temperatures in the Northern parts of South Asia are usually much higher in summer and the effect on COVID-19 transmission and mortality remains to be seen. A recent study in India found an effect of temperature and humidity on incidenceofCOVID-19, however the effect was variable in different states [80].

Ultraviolet Radiation: There is a possibility of ultraviolet (UV) B radiation influencing COVID-19 cases and fatality because of its effect on vitamin D synthesis. An analysis of data covering 108 days from 22 January 2020 until 8 May 2020 across 183 countries found that one unit increase in UV index is associated with a 1.2 percent decline in daily growth rates of cumulative COVID-19 deaths ($p < 0.01$) [81]. South Asia having high UV B exposure which usually peaks between June and September could see reduction in growth rate of cases in coming weeks.

b. Effect of environmental factors on virus: In a study of the viability of SARSCoV, the dried virus on smooth surfaces retained its viability for over 5 days at temperatures of 22–25 °C and relative humidity of 40–50% (which is a typical air-conditioned environment). However, virus viability was rapidly lost at higher temperatures (38 °C) and higher relative humidity (95%) [82].Airborne human coronavirus 229E was found to have a half-life of 67 h at a RH of 50% at a temperature of 20 °C, while it was only about 3 h at RH of 80% at the same temperature [83]. High temperatures and humidity are typically seen in monsoon season in South Asia.

c. Effect of environmental factors on host response: Temperature and daylight hours have been seen to have effect on various aspects of the immune response. Significantly increased pro-inflammatory transcriptome (e.g. enhanced levels of soluble IL-6 receptor and C-reactive protein along with increased expression genes associated with pro-inflammatory processes) were seen in winter compared to summer in a study in Europe [84].The possibility of high temperatures in South Asia influencing the host immune response cannot be ruled out.

5. Public health response

Countries in South Asia, especially India implemented early social distancing measures along with restrictions on international flights, public transport, school closures and "lockdown'. In an analysis of data from 12 countries, countries implementing early lockdowns had better reduction in growth rate of confirmed cases and deaths compared to those which implemented lockdowns late [85]. Strong associations were found for restrictions of mass gatherings (RRR 0.65, 95% CI 0.53–0.79), school closures (RRR 0.63, 95% CI 0.52–0.78) and measures of social distancing (RRR 0.62, 95% CI 0.45–0.85) in the study of 375,609 cases from all over the world [79]. The effect of implementation of early containment measures in India cannot be overlooked.

6. Conclusion

Despite a recent surge in the incidence of confirmed cases of COVID-19 in South Asia, the incidence and mortality in proportion to the population size is lower than in Western Europe and North America. Multiple biological factors, environmental conditions and public health response have all likely contributed to this trend; however there is a need of basic, clinical and epidemiological research from this part of the world to understand these variations better. Data on prevalence and mortality in coming weeks and months will improve our understanding of behaviour of COVID-19 in South Asians.

Author Contribution

RG and AM planned the outline. RG reviewed the literature and wrote the manuscript. RG and AM edited the manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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